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PUBLIC HEALTH AND PREVENTIVE ASPECTS OF STREPTOCOCCAL INFECTIONS*

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MANY aspects of respiratory infection by hemolytic streptococci have become better understood during the last ten years. The development of technique for the serological classification of these organisms has implemented clinical and epidemiological studies of great importance. A variety of immunological procedures have also contributed valuable information. The rapid mobilization of troops in the present war led to outbreaks of streptococcal infection in certain areas which permitted the establishment of comprehensive programs for the study of the nature of disease caused by these organisms and its control.

STUDIES MADE DURING LAST DECADE

The results of the work of the last decade may be summarized: 1. Hemolytic streptococcal respiratory infections are nearly always caused by organisms that are members of a single serological group, designated by the letter "A"[1] A large number of types have been identified within this group. When typing[2] is performed, it is discovered that, during any season in any community, a relatively small number of different types will be responsible for nearly all infections, both respiratory and non-respiratory.

2. There is no essential difference between hemolytic streptococcal sore throat with (scarlet fever) and without rash. It is true that the average example of the former disease is somewhat more ill than the latter, but there is much overlapping. The incidence of serious complications is similar in both types of disease. Recent studies indicate that there are many types or strains of streptococci that are unable to induce rash formation in susceptible individuals, but do produce important and disabling disease. Because of this fact, and because many individuals have immunity to the erythrogenic toxin, infection without rash formation occurs much more frequently and is more important.

3. The character of hemolytic streptococcal respiratory disease is variable. In children less than two years of age it lacks the explosive qualities which it assumes in later life, tends to produce chronic suppurative processes, rash formation is uncommon, and arthritic complications are rare.[3] In older children and adults, streptococcal infection of the upper respiratory passages is often an acute febrile illness associated with exudative tonsillitis, redness and edema of the pharyngeal tissues, tender anterior cervical adenitis, leucocytosis, and a rapid erythrocyte sedimentation rate. Many atypical, mild, and even inapparent infections occur and it is quite possible that they are comparable in number with clinically recognizable cases.

4. Group A hemolytic streptococcal respiratory disease is frequently followed by non-suppurative complications that are probably the result of a complex immunological mechanism.[4] Approximately 20 per cent of infections in adults are followed by continuing disease processes. In some individuals the erythrocyte sedimentation rate remains rapid for several weeks, frequently with clinical evidence of continuing disease in the form of fever and malaise. Electrocardiographic evidence of carditis may be demonstrated in many of these cases. In a rather small group arthritis will appear in addition to the signs and symptoms just described. *A recent critical study[4] revealed that the syndrome usually described as "rheumatic fever" occurred only as a sequel to infection by Group A hemolytic streptococci.* The results of these observations were summarized as follows:

"It seems quite impossible to establish adequate criteria for the accurate division of these various late complications of streptococcal disease into separate groups. Instances of carditis with and without arthritis must be regarded as comparable disorders, and both appear to be related to arthritic disease without carditis. Since arthritis has been demonstrated without carditis and the reverse, there appears to be no valid reason for concluding that examples of continuing disease in the absence of both of these clinical phenomena are unrelated to the first two types of disorder.

"Because of these difficulties, and because evidence of carditis, the most serious complication, was observed most frequently in the absence of arthritis, it would seem to be desirable to discourage the emphasis placed on the syndrome "rheumatic fever" and to begin to think in terms of the complications occurring after streptococcal infection, which might well be called the "post-streptococcal state." Such disorders as "rheumatic fever," "post-scarlatinal arthritis," "atypical rheumatic fever," and others, could be considered as a single entity. Furthermore, the fact that serious non-arthritic complications may follow streptococcal infections would be emphasized."

The background just presented indicates the importance of hemolytic streptococcal respiratory infection. Much disability results from the acute illness and the suppurative complications which occasionally follow. Suitable therapy, when indicated, with penicillin or the sulfonamides may be expected to minimize this problem. No proved technique is yet available for the treatment of established hemolytic streptococcal infections which will prevent the development of the serious late non-suppurative complications that are so frequently followed by chronic valvular heart disease. Furthermore, the vast number of mild and inapparent infections will not ordinarily receive medical attention, but are potentially capable of inciting the most severe arthritic and non-arthritic complications.

It is clear, therefore, that the elimination of rheumatic fever and the related disorders associated with the post-streptococcal state requires, in the light of our present information, *the complete suppression of infection of human beings by hemolytic streptococci.* The magnitude of the national problem needs no additional emphasis when it is realized that streptococcal respiratory disease and its complications have been one of the principal causes of disability in many military training establishments, and that acute rheumatic fever and chronic valvular heart disease are, next to tuberculosis, the most frequent causes of death due to infectious disease among children and young adults.

Various techniques are of potential value in the prevention of infection by hemolytic streptococci which may

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be described and evaluated. They fall naturally into two groups.

PREVENTION OF TRANSMISSION

The most widely applied methods for the prevention of respiratory infections have been those designed to prevent the transmission of the etiological agent from the infected individual or healthy carrier to susceptible persons. These must be discussed with special reference to streptococcal disease.

1. *Isolation of Infected Cases.*—The isolation of individuals suffering from respiratory infections of all sorts as a control measure has, in general, failed to be of value. It has been particularly futile in relationship to streptococcal disease, since nearly all public health departments require the isolation of scarlet fever, but ignore the many examples of similar disease without rash that are fully capable of transmitting infection. When it is further understood that virulent organisms persist in the nasopharynx for many weeks after recovery, and that inapparent and unrecognized cases are very frequent, it is obvious that isolation of sick persons will not prevent the spread of streptococcal disease.

2. *Control of Carriers.*—The problems involved in the control of healthy carriers of Group A hemolytic streptococci become apparent when it is realized that from five to fifty per cent of all persons may harbor these organisms in the nasopharynx. The rate will vary with age, the presence or absence of tonsils, and the epidemic state of the community. No satisfactory procedure for the elimination of hemolytic streptococci from the throats of carriers has been devised. Sulfonamides and the local application of various antibiotics have not been useful. Prolonged administration of penicillin may be effective but is, as yet, extremely cumbersome. Other natural factors are at work, however, which in part reduce the hazard arising from the presence of large numbers of carriers. It is possible that the invasiveness of the organism may be reduced by prolonged residence in the throat, or by other unknown mechanisms. More important are recent observations[5] which indicate that individuals are "dangerous carriers" only if they harbor hemolytic streptococci in the nose. Such persons disseminate into their environment many more streptococci than do simple throat or tonsillar carriers. The elimination of nasal carriers from operating rooms, kitchens and other institutional situations may be of value.

3. *Sterilization of Air.*—Considerable evidence exists which suggests that hemolytic streptococci may be "airborne" and produce infection at points remote from their source. If this is correct, it would be desirable to prevent such spread by removal of bacteria from the air. Three methods are available at present for this purpose.[5] One involves the reduction of air contamination by the oiling of floors and bedding. It has been demonstrated that it is possible to greatly decrease the number of bacteria including hemolytic streptococci that will be disseminated into the air from secondary extra human reservoirs during such activities as floor sweeping, bed making, and dressing.

Two techniques are also available for the sterilization of air. In one, the bactericidal properties of ultra-violet light are utilized; in the other, those of certain glycols that may be vaporized into the air.

All of these methods are under study at the present time and it is not yet possible to evaluate their effectiveness in the reduction of the transmission of streptococcal disease. It is quite apparent, however, that certain mechanical limitations to their usefulness exist. They are relatively cumbersome and expensive, and will probably only be applicable under circumstances in which numbers of persons are congregated for work or amusement within enclosed spaces such as factories, theaters, auditoriums, ships, and in military establishments.

Most important, however, is the fact that the prevention or control of contamination of the air by hemolytic streptococci can not be expected to eliminate the transmission of disease by direct contracts between infected cases and carriers, and susceptible individuals.

PREVENTION OF TISSUE INVASION

Because the available methods do not eliminate the transmission of hemolytic streptococci from carriers and infected cases to the respiratory passages of susceptible human beings, it has been necessary to seek means for the prevention of tissue invasion and the establishment of disease by these organisms after they have reached the nasopharynx.

1. *Chemoprophylaxis.*—An extensive experience in civilian practice[7] and in the armed forces[8,9] had apparently established the effectiveness of sulfonamides as prophylactic agents for the prevention of hemolytic streptococcal respiratory disease. The daily administration of one gram of sulfadiazine almost completely eliminated this type of infection in a large group of highly susceptible military personnel and greatly reduced the frequency of occurrence of rheumatic fever. A similar program usually prevented recurrences of activity in children who had undergone previous attacks of acute rheumatic fever. Protection was presumably lost within a few days after the discontinuation of continuous chemoprophylaxis. More recent observations indicate that a considerable number of sulfonamide resistant strains of Group A hemolytic streptococci are prevalent in certain population groups and that their epidemic spread is not affected by chemoprophylaxis. The usefulness of this technique for the prevention of hemolytic streptococcal respiratory disease has not, therefore, been completely evaluated.

Toxic reactions, following the prolonged use of sulfonamide prophylaxis by the Navy, have been few. Approximately 0.5 per cent of adult males, who received one gram of sulfadiazine per day, developed a dermatitis which disappeared promptly when the drug was withdrawn. Serious complications, such as exfoliative dermatitis and granulocytopenia were observed in only 0.01 per cent. These untoward reactions were ordinarily reversible if no further sulfonamide was administered. These experiences make it proper to recommend sulfonamide prophylaxis under circumstances in which it is essential that hemolytic streptococcal respiratory infection be prevented, since the degree of protection may be high and the incidence of toxic reactions is low. Such situations will arise in the armed forces, in rheumatic subjects, in schools and institutions, and perhaps even in whole communities if streptococcal disease should become epidemic. The possible presence of sulfonamide resistant strains must be constantly borne in mind. The epidemic streptococci should be tested *in vitro* and chemoprophylaxis established only if the organisms are definitely inhibited by low concentrations of sulfonamides.

It is of great importance that sulfonamide prophylaxis *never be undertaken unless all of the subjects receiving the drug are readily available for frequent examination by a physician.* A careful history must be obtained and *the drug withheld from all persons in whom evidence of a previous sulfonamide sensitivity is discovered.*

2. *Biological prophylaxis.*—It does not seem probable that the most complete control of carriers and infected cases, and the most extensive application of air sterilization now anticipated, will result in a great reduction in the frequency of hemolytic streptococcal respiratory disease and its complications. The use of chemoprophylaxis

is also impractical in other than selected and carefully controlled groups.

Some other method must therefore be sought which will raise the resistance of the individual to infection by streptococci. The establishment of active immunity by vaccines is an obvious possibility but is fraught with many difficulties. Considerable evidence exists to indicate that immunity is type-specific. Since many serological types are constantly causing disease, polyvalent vaccines would be required. It also seems quite possible that any increased resistance to infection would be short lived. There is, in addition, the real possibility that inoculation of human beings with these organisms would increase the streptococcal tissue sensitivity and enhance the opportunity for the development of post-streptococcal complications in such persons, if subsequent infection should occur.

The biological prevention of hemolytic streptococcal infection should certainly be explored, but it is unlikely that a satisfactory prophylactic technique will be established.

SUMMARY

Respiratory disease caused by hemolytic streptococci is of extreme importance because disability results not only from the acute illness but also from the serious non-suppurative complications which frequently follow. Rheumatic fever is one of these but is only part of a complex pathological process initiated by infection by streptococci.

Measures for the prevention of transmission at the present time include isolation and control of infected cases and carriers, air sterilization, and chemoprophylaxis. Each of these is applicable only under special circumstances. No technique has been suggested which appears likely to succeed in the principal problem, which is the elimination of infection by streptococci from the whole population.

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More Boys Than Girls Are Born During War

It is true that more boys than girls, proportionately, have been born in war years, particularly in the years after a war, according to Dr. George Wolff, U. S. Children's Bureau statistician, but why it is true nobody knows.

Dr. Wolff advances several theories. It may be that the younger age of the mothers has something to do with it since in war periods more people get married and at a younger age. Or it may be the younger age of the father or some other biological reason.

Normally, the sex ratio is between 105 and 106 boys born for every 100 girls. In war years the sex ratio may go up to 107 or 108, a rise sufficient to have significance. Among Negroes in the United States, the differential is less than for whites, only about 102 boys being born for every 100 girls.

CARCINOMA OF THE RECTUM*

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OF the cancers of the body, cancer of the rectum ranks number four in frequency, and kills 9,000 persons every year in the United States, according to the Federal Bureau of Vital Statistics. There is an apparent, if not a true, increase in the incidence of cancer of the rectum. In the report of the Federal Bureau of Vital Statistics for the year 1882, which recorded 204 cases of deaths from cancer of the rectum, it is stated "cancer is a disease which is believed to be gradually increasing in frequency and causing a large proportion of deaths in those nations which are most advanced in civilization." In 1890 there were 574 deaths in ratio of 2 per 100 000 population. In 1940 the ratio was 6.7 per 100.000. The death rate is too high because too many patients receive treatment too late. The early lesion exhibits few, or no signs or symptoms, and the patient does not recognize gradual changes from his normal state of well being. The physician may fail to make a manual or proper sigmoidoscopic examination, may regard a negative finding from the barium enema as conclusive, make a diagnosis of diverticulitis, so-called "mucus colitis, amoebiasis, chronic ulcerative colitis, etc.," or give treatments of "shots" for hemorrhoids.

The majority of these patients with cancer are between the ages of 50 and 70, but 20 per cent occur before the age of 50. About 3 per cent occur between the ages of 20 and 30, and it is in this decade of life that they are most often overlooked. Cancer in the young, as a rule, is highly malignant, metastasizes rapidly and the majority of these individuals are inoperable when seen, or die with metastases.

DIAGNOSIS

The common signs and symptoms are a change in bowel function, especially frequency, which is so often called diarrhoea, or dysentery, unsatisfied stool with blood or mucus, abdominal discomfort, and in some cases evidence of obstruction as increasing constipation. Pain is absent or late.

Proper palpation will reveal 80 per cent. The sigmoidoscopic examination will complete the diagnosis. The lesion may be a polyp or polypoid mass, a crater-like ulcer with firm margins, or an annular lesion involving all of the bowel. A biopsy specimen should be examined for confirmation, and if negative, should be repeated. Sigmoidoscopic examination should be done under intravenous anesthesia if the instrument cannot be passed to 8 inches, especially if blood is a constant finding. The negative opaque enema is valueless below 8 inches and may be dangerously misleading, because a filling defect is usually obscured by other loops of bowel, and for this reason should never be given preceding the sigmoidoscopic examination.

Microscopical grading of the specimen is valuable in adenomas, polyps, and villous papillomas. These are usually a Grade 1, or pre-malignant, if not benign. The grading of frank adenocarcinomas should not influence the treatment because radical removal is indicated whether or not the Grade is II, III, or IV.

Differential diagnosis must be made from sarcomas (rare), metastasis from upper abdominal lesions (stomach, pancreas, ovary, uterus, bladder, colon), and prostate, from radium burn, and chronic infections as

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